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Transplanted human forebrain assembloids for neural activity readouts and functional maturation

Stanford researchers have developed an innovative platform that enables transplantation of human forebrain assembloids into the rodent brain, supporting advanced neuronal maturation and functional neural activity readouts.

Human stem cell-derived brain organoids and assembloids are widely used to study neural development and disease. However, when grown in vitro, these models lack key features of the living brain, including coordinated neural activity, sensory input, and functional circuit integration, which limits their maturation and physiological relevance.

This technology introduces a method to generate and transplant human forebrain assembloids containing both excitatory (glutamatergic) and inhibitory (GABAergic) neurons into the developing rodent cortex. Following transplantation, the assembloids grow substantially, integrate with host neural circuits, and mature at molecular, structural, and electrophysiological levels beyond what is achieved in vitro.

Importantly, the transplanted human neurons participate in functional neural networks, enabling system-level activity measurements such as electrophysiological recordings and responses to sensory inputs. In some cases, these integrated circuits can influence host brain activity, providing a more complete model of human neural function.

By combining human-specific cellular models with in vivo integration and functional readouts, this platform provides a more physiologically relevant system for studying brain development, neuropsychiatric disorders, and therapeutic responses.

Applications

- Drug and therapeutic testing in human-relevant neural systems
- Modeling human brain development and neuropsychiatric disorders
- Functional analysis of human neural circuits in vivo
- Evaluation of neural activity using electrophysiological readouts (e.g., EEG)

Advantages

- Enables in vivo transplantation of intact human forebrain assembloids
- Promotes maturation of inhibitory interneurons, including fast-spiking (PV) subtypes
- Supports physiologically relevant neural activity and circuit dynamics
- Allows system-level electrophysiological measurements (e.g., EEG)

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